

### **REMARKS**

Please reconsider the application in view of the amendments above and the following remarks. Applicant thanks the Examiner for carefully considering this application.

#### **Disposition of the Claims**

Claims 1, 5-7, and 22-25 are pending. Claim 1 is independent. The remaining claims depend, directly or indirectly, from claim 1.

#### **Claim Amendments**

Claims 1, 5 and 6 have been amended to correct informalities. No new matter is introduced by these amendments.

#### **Claim Objections**

Claims 1, 5, and 6 are objected to because of informalities.

Claims 1, 5, and 6 have been amended to correct these informalities. Accordingly, withdrawal of this objection is respectfully requested.

#### **Rejections under 35 U.S.C. § 112**

##### **Claims 1, 5-7, and 22-25**

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner considers that limitation “under pH 5 to 6” of claim 1 is indefinite. Claim 1 has been amended to recite, *inter alia*, “under a condition of pH 5 to 6.” Therefore, claim 1 is not indefinite. The remaining dependent claims should not be indefinite for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

Claim 5

The Examiner points out that the limitation “at least sugar residues” of claim 5 is indefinite. Claim 5 has been amended to recite, *inter alia*, “at least 6 sugar residues,” which was recited in the previous claim set (*see*, for example, Applicant’s response to Office Action dated April 7, 2009). Therefore, claim 5 is not indefinite. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1, 5-7, and 22-25

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner asserts that, while the specification, e.g., paragraph [0141], describes the benzyl protection at pH 5 to 6, the specification does not support allyl or diphenylmethyl protection at pH 5 to 6, thus, introducing new matters.

When a disclosure describes a claimed invention in a manner that permits one skilled in the art to reasonably conclude that the inventor possessed the claimed invention the written description requirement is satisfied. (MPEP §2163).

The specification teaches that, to prevent the sialic acids from being cut off by an acid, the carboxyl group of a sialic acid may be protected by a protective group, such as benzyl, allyl, or diphenylmethyl. (Paragraph [0125]). These protecting groups can be put on using the corresponding halides or other leaving groups. The allylic and benzylic positions, being next to an unsaturated bond, are much more reactive than analogous alkyl halides. For example, allyl bromide is about 33 times more readily substituted than ethyl bromide. In most organic textbooks, allyl and benzyl compounds are often discussed together. A skilled artisan would recognize that these (allylic or benzylic) groups can often substitute for one another in the same reactions.

The carboxyl group of a sialic acid is deprotonated (ionized) under a mild acidic condition, such as pH 5 to 6. The ionized carboxylate is a mild nucleophile, which can readily react with an allylic or benzylic halide compound, resulting in the protection of the carboxyl group, as illustrated in paragraph [0141] using benzyl bromide. These reactions are well known in the art. See for example, "Protective Groups in Organic Chemistry," John Wiley & Sons Inc., New York 1991, ISBN 0-471-62301-6. (Paragraph [0126]). A skilled artisan would know that benzylic and allylic substitutions occur under similar conditions. Therefore, demonstration of one (benzylic substitution) would indicate that other groups (e.g., allylic and diphenylmethyl groups) can also be reacted in a similar manner. In other words, one skilled in the art can reasonably conclude that the inventor possessed the claimed invention with allyl or diphenylmethyl analogs. Accordingly, withdrawal of this rejection is respectfully requested.

**Rejections under 35 U.S.C. § 103(a)**Claims 1, 5-7, and 22-25

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns (J. Chem. Soc. Perkin Trans. 1, 1998, pages 549-560, PTO-1449 submitted December 20, 2007) (hereinafter “Meinojohanns”) in view of Keil, et al. (Angew. Chem. Int. Ed., 40, No. 2 (2001), pp. 366-369) (hereinafter “Keil”) and Greene, et al. (Protective Groups in Organic Synthesis, Third Edition, John Wiley & Sons, Inc. (1999); pp. 415-419) (hereinafter “Greene”). Claim 1 has been amended. To the extent that this rejection may still apply to the amended claims, this rejection is respectfully traversed.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be shown or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ (C.C.P.A., 1074)

The present invention is related to processes of preparing a glycopeptides having asparagine-linked oligosaccharides at a desired position of the peptide chain. Specifically, claim 1 requires, *inter alia*, “preparing an asparagine-linked disialooligosaccharide or an asparagine-linked monosialooligosaccharide having amino group nitrogen protected with a fat-soluble protective group and the carboxyl group of the sialic acid protected with a benzyl, allyl, or diphenylmethyl group, wherein the benzyl, allyl, or diphenylmethyl group is introduced into the carboxyl group of the sialic acid under a condition of pH 5 to 6.”

Meinojohanns teaches processes of making N-linked glycoproteins using oligosaccharide-asparagine building blocks. (Page 555, Scheme 4). The glycoproteins, which contain the oligosaccharide-asparagine building blocks, will then be subject to an enzymatic reaction using sialyltransferase to directly introduce the sialyl moieties into the peptide. (Page 556, Scheme 5). In other words, Meinojohanns does not use pre-made asparagine-linked disialooligosaccharides or asparagine-linked monosialooligosaccharides in the processes.

Further, Meinojohanns does not teach or suggest that the step of protecting the carboxyl group of sialic acid after the sialyltransferase reaction, because the glycopeptides are not further extended. (Page 556, Scheme 5; and page 560, left column).

Therefore, Meinojohanns fails to teach, "preparing an asparagine-linked disialooligosaccharide or an asparagine-linked monosialooligosaccharide having amino group nitrogen protected with a fat-soluble protective group and the carboxyl group of the sialic acid protected with a benzyl, allyl, or diphenylmethyl group, wherein the benzyl, allyl, or diphenylmethyl group is introduced into the carboxyl group of the sialic acid under a condition of pH 5 to 6," as required by claim 1.

Kiel teaches the use of the threonine-linked sialooligosaccharide as a build block to synthesize glycopeptides. (Page 367, Scheme 1). In particular, Kiel teaches a threonine-linked sialooligosaccharide build block, in which both the carboxyl group of sialic acid and the carboxyl group of threonine are protected. In contrast, the present invention teaches that, at pH 5

to 6, only the carboxyl group of sialic acid (and not the carboxyl group of asparagine) of the asparagine-linked sialooligosaccharide is selectively protected.

Therefore, Kiel fails to teach or suggest what is missing in Meinojohanns, i.e., “preparing an asparagine-linked disialooligosaccharide or an asparagine-linked monosialooligosaccharide having amino group nitrogen protected with a fat-soluble protective group and the carboxyl group of the sialic acid protected with a benzyl, allyl, or diphenylmethyl group, wherein the benzyl, allyl, or diphenylmethyl group is introduced into the carboxyl group of the sialic acid under a condition of pH 5 to 6,” as required by claim 1.

Greene teaches a method for protecting the  $\beta$ -carboxyl group of aspartic acid. Particularly, Greene teaches an ester formation between the  $\beta$ -carboxyl group of aspartic acid and a benzyl alcohol by heating a solution in the presence of 12 M HCl. (Page 416, Entry 5). This is an acid catalyzes dehydration (esterification) between an acid and an alcohol. In the presence of 12 M HCl, a skilled artisan would know that various hydroxyl groups (such as those on sialic acids or carbohydrates) would also react, without selectivity, with the carboxyl groups. More importantly, under this condition (12 M HCl), the sialic acid on polysaccharides would be cleaved. Therefore, the process of Greene cannot be used to selectively protect a carboxyl group of a sialic acid on a polysaccharide, and 12M HCl (pH < -1) is not the same as under a condition of pH 5 to 6.

For reasons set forth above, Meinojohanns, Kiel, and Greene, whether considered separately or in combination, fail to teach or suggest the step of “preparing an asparagine-linked disialooligosaccharide or an asparagine-linked monosialooligosaccharide having amino group nitrogen protected with a fat-soluble protective group and the carboxyl group of the sialic acid protected with a benzyl, allyl, or diphenylmethyl group, wherein the benzyl, allyl, or diphenylmethyl group is introduced into the carboxyl group of the sialic acid under a condition of pH 5 to 6,” as required by claim 1.

Therefore, claim 1 is patentable over Meinojohanns in view of Kiel and Greene. Dependent claims 5-7 and 22-25 should also be patentable for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1, 5-7, and 22-25

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto (Angew. Chem. 2003, 115, 2641-2644, published online June 5, 2003) (hereinafter “Yamamoto”) in view of Meinojohanns.

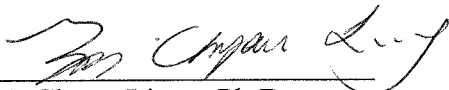
Yamamoto was published on June 5, 2003, which is after the priority date of the present application, i.e., November 29, 2002. An English translation of the priority document, Japanese Patent Application No. JP2002-349166, is attached herewith. Therefore, Yamamoto does not qualify as a prior art reference against the present invention. Accordingly, withdrawal of this rejection is respectfully requested.

**Conclusion**

Applicant believes this reply is fully responsive to all outstanding issues and places this application in condition for allowance. If this belief is incorrect, or other issues arise, the Examiner is encouraged to contact the undersigned or his associates at the telephone number listed below. Please apply any charges not covered, or any credits, to Deposit Account 50-0591, Reference 17563/003001.

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Respectfully submitted,

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Attachment: English translation of Priority Document